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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,860	01/06/2006	Hana Golding	65831 (47992)	4611
46037 7590 05/12/2010 EDWARDS ANGELL PALMER & DODGE LLP PO BOX 55874 BOSTON, MA 02205				
EXAMINER				
CHIEN, STACY BROWN				
ART UNIT		PAPER NUMBER		
1648				
MAIL DATE		DELIVERY MODE		
05/12/2010		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/536,860

Applicant(s)

GOLDING, HANA

Examiner

Stacy B. Chen

Art Unit

1648

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 March 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5,7,12-15,17,18 and 21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5,7,12-15,17,18 and 21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 May 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's remarks filed on March 4, 2010 are acknowledged. Claims 1, 5, 7, 12-15, 17, 18 and 21 are pending and under examination.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5, 7, 12-15 and 17 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Domínguez *et al.* (*Journal of Immunological Methods*, 1998, 220:115-221, "Domínguez") in view of Hooper *et al.* (US Patent 6,451,309, "Hooper").

Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that the instant method is directed to a novel neutralization assay that measure protection of cells against virus invasion. Applicant notes that the specification teaches that the action of an antibody binding to a pathogen that disallows productive infection is neutralization.
- In response to Applicant's assertion that the claims are directed to a neutralization assay, the Office notes that only claim 14 recites the term "antibody". As stated by Applicant and in the specification, neutralization specifically involved

antibodies. Since claims 1, 5, 7, 12, 13, 15, 17, 18 and 21 do not specifically recite "antibodies", they are not by definition, neutralization assays.

- Applicant argues that it would not have been obvious to use monoclonal antibodies (taught by the Hooper reference) in the methods of Domínguez, because Domínguez only teaches recombinant vaccinia expressing GFP for detection of cells by flow cytometry. Applicant points out that Domínguez is concerned with a method to identify potential targets and cell tropism of the virus, but does not teach a method to measure protection of cells against virus invasion by measuring a decrease in invasion by a candidate agent.
- In response to Applicant's argument, the Office is aware of the limitations of the Domínguez reference concerning the missing candidate agent aspect. However, the obviousness rejection of record sets forth that it would have been obvious to use the vaccinia-GFP construct of Domínguez to test the infectivity of cells in the presence of Hooper's monoclonal antibodies to determine whether the antibodies are effective agents that inhibit vaccinia virus infectivity (*i.e.*, decrease of viral entry as a result of binding, or as Applicant may prefer, "neutralization", with the monoclonal antibody). One would have been motivated to use the vaccinia-GFP construct because it shows infectivity, not merely neutralization. As is taught by Hooper, neutralization tests were not always predictive of protective efficacy in mice upon challenge (Hooper, col. 2, lines 14-20). One of ordinary skill in the art would have been motivated to use a method that better reflects the inhibiting activities of the monoclonal antibodies (decrease of viral entry as a result of

binding with the monoclonal antibody), such as the method described by Domínguez.

- Applicant argues that the combined teachings do not arrive at the claimed method that measures protection of cells against virus invasion by measuring a decrease in invasion by a candidate agent.
 - In response to Applicant's argument, the combined teachings result in a method that looks at the ability of an antibody to interfere with the infection of cells by using a vaccinia virus/GFP infection marker. This translates to a method that measures protection of cells (*i.e.*, whether the antibody interferes with infection) against virus invasion (*i.e.*, vaccinia/GFP construct) by measuring a decrease in invasion (*i.e.*, determined by flow cytometry) as a result of the activity of a candidate agent (*i.e.*, an antibody).
- Applicant asserts that the present method provides a prediction of virus lethality, which is not possible with the individual or combined teachings of Domínguez and Hooper. Applicant argues that the Hooper reference does not teach or suggest a reporter-based assay that demonstrates the protective activity of their monoclonal antibodies. Applicant points to page 10 of the specification and Example III, which discloses that *in vitro* neutralization assays are predictive of lethality.
 - In response to Applicant's arguments, the specification discloses that a mouse lethality model (SCID mice) was used to show that *in vitro* neutralization assays correlated positively with significant difference in protective efficiency against lethal infection of mice with vaccinia. The ability of the *in vitro* neutralization

assay as a predictor of virus lethality has nothing to do with the claimed method because there is no limitation in the claims regarding predicting lethality. The claimed method is what it is, regardless of further implications of performing the method. In other words, subsequent method steps that can be performed as a result of carrying out the claimed method, are not part of the claimed method.

- The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Therefore, the invention remains obvious over the prior art to one of ordinary skill at the time of the invention.

3. Claims 18 and 21 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Domínguez *et al.* (*Journal of Immunological Methods*, 1998, 220:115-221, “Domínguez”) in view of Hooper *et al.* (US Patent 6,451,309, “Hooper”) as applied to claims 1 and 17 above, and further in view of Engelmayer *et al.* (*The Journal of Immunology*, 1999, 163:6762-6768, “Engelmayer”). Applicant’s arguments regarding this rejection have been addressed above. The rejection is maintained for reasons of record.

Conclusion

4. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30), alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B Chen/
Primary Examiner, Art Unit 1648